Model of the cerebral venous return

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Introduction: Within the multiple sclerosis (MS) research community the concept of chronic cerebrospinal venous insufficiency (CCSVI) has caused much controversy, and this has led some researchers to challenge the findings of Zamboni *et al* [1]. In particular, Doepp *et al* found no evidence of CCSVI in MS patients [2]. However, no hydrodynamic analysis was performed on the blood flow data collected during this study. Independent analysis of Doepp *et al*'s data by Beggs [3] suggested that contrary to Doepp *et al*'s assertions, the study actually revealed severe venous abnormalities in MS patients. In this paper, Beggs' initial hydrodynamic analysis is expanded using a simple model of the extracranial venous system.

Materials & Methods: This paper uses a simple hydrodynamic model of the extracranial venous system to interpret Doepp *et al*'s blood flow data. In particular, analysis is undertaken of the impact that extracranial venous stenosis has on cerebral blood flow (CBF) in the upright position.

Results: Hydrodynamic analysis of the data indicates that, when upright, the MS patients in Doepp *et al*'s study exhibited considerable rerouting of the extracranial venous blood flows compared with health controls. This suggests that in these patients venous stenosis was present, resulting in extensive collateral rerouting of the blood flow back to the heart. The results also indicate that there is a strong postural component to be abnormalities observed.

Discussion & Conclusion: Extensive collateral rerouting to the venous blood flow from the brain is something that has been observed by Zamboni *et al* [4]. Although this rerouting will help to relieve intracranial venous hypertension, stenosis of the extracranial venous pathways will inevitably increase the overall hydraulic resistance of the cerebral vascular circuit. Increasing the system resistance will have a dual effect; firstly, it will tend to reduce cerebral blood flow (CBF), and secondly, it will raise the

pressure in the venous sinuses [1]. Evidence supporting the former conclusion comes from several studies [5-7], all of which observed lower CBF in the normally appearing white matter of MS patients compared with healthy controls, particularly in the periventricular region. While no published data exists regarding blood pressure in the venous sinuses of MS patients, indirect evidence of hypertension in these vessels comes from two studies [8, 9]. In the first of these, Zamboni *et al* observed that following angioplasty to open up stenotic vessels, the venous pressure in MS patients dropped by approx. 2.2 mm Hg [8]. In the second study [9], Zamboni *et al* found that the bulk flow of the CSF in MS patients was greatly reduced compared with healthy controls; something that is indicative of raised blood pressure in the SSS.

Doepp *et al*'s data appear to confirm that there may be a postural element in the pathophysiology of MS. Previous researchers have observed abnormal heart rate and blood pressure responses in MS patients during tilt table tests and have attributed this to cardiovascular autonomic regulation failure [10, 11]. Flachenecker *et al* [12] found that fatigue in MS patients correlated with autonomic dysfunction and postulated that that this was possibly due to lesions impacting on the a sympathetic vasomotor. However, while these investigators performed standard autonomic control tests on MS patients, none measured the changes in the extracranial venous flow rate that occur when subjects move from the supine to upright position. When supine, the IJVs generally act as the principle route by which blood drains from the brain, whereas when upright, their role becomes minimal, with the vast majority of the blood traveling either down the VVs or through other venous pathways [13, 14]. In Doepp *et al*'s study both cohorts conformed to this norm when supine, whereas only the healthy controls did when upright – a situation that is highly unusual. Doepp *et al*'s results therefore suggest that, rather than any autonomic cause, the rerouting of blood in MS patients occurs as a result of stenosis which primarily affects the venous pathways that are normally used to transport blood back to the heart when upright.

References: (1) Zamboni et al. *J Neurol Neurosurg Psychiatry* 80:392, 2209. (2) Doepp et al. *Ann Neurol* 68:173, 2010. (3) Beggs. *Ann Neurol* 68:560, 2010. (4) Zamboni et al. *Curr Neurovasc Res* 6:204, 2009. (5) Law et al. *Radiology* 231:645, 2004. (6) Varga et al. *J Neurol Sci* 282:28, 2009. (7) Adhya et al. *Neuroimage* 33:1029, 2006. (8) Zamboni et al. *J Vasc Surg* 50:1348, 2009. (9) Zamboni et al. *Funct Neurol* 24:133, 2009. (10) Saari et al. *Clin Neurophysiol* 115:1473, 2004. (11) Kanjwal et al. *Int J Med*

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